Please add the additional claim:

102. (added) The composition of proliferating dendritic cell precursors according to claim 82 further comprising GM-CSF.

REMARKS

Claims 82-101 are pending in the application. Claims 86-88, 90-93, 98, and 100 are withdrawn as relating to a non-elected group. Claims 82-85, 89, 94-97, 99, and 101 are rejected.

Claim 83 has been cancelled. Claims 82, 84, 89, 94, 96 and 101 have been amended. Additional claim 102 has been added.

Claims 84, 89 and 94 have been amended to correct the pendency of the claims based on the Examiner's objection to those claims.

Claim 82 has been amended to more clearly claim applicants' invention. Support for the amendment to claim 82 can be found throughout the specification, see for example, page 8, lines 13-27, as well as page 29, lines 21-23; page 35, lines 25-27; and page 37, lines 17-18

Support for the amendments to claims 96 and 101 can be found at page 29, lines 21-23; page 35, lines 25-27; and page 37, lines 17-18. Claim 96 has also been amended to conform to claim 82.

Support for additional claim 102 can be found in original claim 82.

A marked up version of the amended claims is attached to this response as Exhibit 1 .

No new matter is added.

Rejections Under 35 U.S.C. § 112, second paragraph

Claim 99 is rejected under 35 U.S.C. §112, second paragraph, because the Examiner contends that the recitation of milligrams of antigen per dose is unclear because "it is unclear how many pulsed cells comprise a dose." According to the Examiner, "there is no relation in the claims of antigen amount to cell quantity or density of antigen density [sic] upon the surface of the cells in the composition". In addition, the Examiner argues that "the claim in reciting a finite amount of antigen without giving any indication what a 'dose' of cells comprises, gives no indication regarding the ability of the 'dose' of dendritic cells to present a sufficient level of processed peptide on their surface for presentation to reactive T cells".

In response, applicants respectfully disagree. The claim is sufficiently clear to allow those skilled in the art to understand the metes and bounds of the claimed subject matter. Claim 99 refers to an amount of antigen applicants consider is preferred to obtain a desired immune response. One skilled in the art would readily be able to determine the actual "dose" or number of dendritic cells necessary to obtain the preferred amount of processed antigen, using standard techniques well known in the art. The specification discloses on page 41, lines 4-8, that the number of antigen-

activated dendritic cells which are reinjected back into an individual in need of treatment may vary depending on, inter alia, the antigen and size of the individual. Moreover, the specification provides guidance regarding the quantity of dendritic cells which would be therapeutically useful, for example, page 41, lines 26-28, provides a range of between 1 $x10^6$ to 10 x 10^6 dendritic cells. Therefore, the specification and claims provide sufficient details regarding preferred dosages such that one skilled in the art could easily adapt the actual dosages using standard techniques. In contrast, the Examiner has not provided any basis for his argument that one skilled in the art would not be able to determine a dose which would fall within the claimed range. In view of this, applicants request withdrawal of this ground of rejection.

The Examiner also rejected Claims 83-85, 89, 94, 95 and 101, as being "ambiguous and unclear in that they are drawn to 'processed antigen presenting dendritic cell precursors' which present antigen in base claim 101". According to the Examiner, the claims are unclear because "once dendritic cells express antigenic fragments on their surface, they are no longer precursors, rather they become mature antigen presenting cells".

Again, the applicants respectfully disagree. The specification makes clear that dendritic cell precursors are capable of expressing and presenting antigen. See, for example, page 10, lines 11-30, or page 36, lines 16-20. Therefore, the claims as drafted are clear and unambiguous. Accordingly, as the Examiner has not provided any basis for his contention, applicants respectfully request that the Examiner withdraw this rejection.

Rejection Under 35 U.S.C. § 102(b)

Claims 82-85, 89, 94-97 are rejected under 35 U.S.C. § 102(b) as being anticipated by Markowicz et al. According to the Examiner, Markowicz et al. teaches the isolation and maturation of dendritic cells from human peripheral blood by the *in vitro* addition of GM-CSF. The Examiner states that "Markowicz et al. teaches that GM-CSF not only increases the survival of dendritic cells *in vitro*, but also stimulates 'DC differentiation to mobile, reversibly adherent cells with long-branched projections'". Therefore, the Examiner concludes that Markowicz et al. anticipates the claimed invention.

In response, the applicants respectfully disagree. Markowicz et al. refers to the isolation and maturation of bone marrow derived dendritic cells using GM-CSF to trigger maturation and/or differentiation of the dendritic cells. In contrast, the present invention is directed to compositions comprising *enriched and expanded* populations of proliferating dendritic cell *precursors* using GM-CSF to stimulate proliferation and expansion of the dendritic cell precursor population. In other words, Markowicz et al. refers to immature dendritic cell populations that are nonproliferating, and are not expanded. Markowicz et al. does not anticipate or suggest applicants' invention. In fact, Markowicz et al. teaches just the opposite of applicants invention, by stating on page 958 that because the total number of dendritic cells in their isolated populations remained stable over time, "...GM-CSF does not cause DC to divide and proliferate." Moreover, Figure 4 of Markowicz et al. shows the lack of an increase in dendritic cell

number over time. Clearly, if a population of dendritic cells were proliferating and expanding as claimed by applicants, this number should increase over time.

Although applicants disagree with the Examiner's 102(b) rejection, to facilitate allowance of the claims, they have amended claims 82, 96, and 101 to recite that the compositions of dendritic cell precursors are expanded. Markowicz et al. does not disclose expanded, proliferating dendritic cell precursor populations; therefore, Markowicz et al. is not an anticipating reference under §102(b). For the foregoing reasons, applicants respectfully request that the Examiner also withdraw this rejection.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account 13-4500, Order No. 2016-4000US5. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: July 3, 2001

By: _____
Kenneth H. Sonnenfeld
Reg. No. 33,285

Mailing Address:

MORGAN & FINNEGAN, L.L.P.
345 Park Avenue
New York, New York 10154
(212) 758-4800
(212) 751-6849 (FAX)

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on July 3, 2001

_____
Kenneth H. Sonnenfeld
Registration No. 33,285

EXHIBIT 1

82. (twice amended) An *in vitro* composition comprising an enriched and expanded population of proliferating dendritic cell precursors [in the presence of GM-CSF].

84. (amended) The composition of dendritic cell precursors according to either one of claim 82 or [83] 101 wherein the dendritic cell precursors are human.

89. (amended) The composition according to claim [83] 101 wherein the antigen is a microorganism.

94. (amended) The composition according to claim [83] 101 wherein the antigen is a mycobacteria tuberculosis bacteria.

96. (twice amended) A pharmaceutical composition comprising a therapeutic amount of an enriched and expanded population of human [dendritic cells] proliferating dendritic cell precursors and a pharmaceutically acceptable carrier.

101. (amended) An *in vitro* composition comprising an enriched and expanded population of processed antigen presenting dendritic cell precursors, wherein said

dendritic cell precursors present processed antigen derived from said dendritic cell precursors contacted *in vitro*, in the presence of GM-CSF, with antigen for sufficient time for said dendritic cell precursors to process and present said processed antigen.